Claims 11 and 16: Currently amended.
Claims 12-15,17 and 18 : Previously presented.
Claims 1-10: Canceled.

DISCLOSURE UNDER 37 CFR §§ 1.97 AND 1.98:

The Applicants hereby submit an Information Disclosure Statement to comply with 37 CFR § 1.98(a). As will be noted, this Information Disclosure Statement calls a number of references, which might be considered relevant, to the attention of the Office. The fact that these are in fact "Prior Art" and/or relevant to the prosecution is, however, not admitted.

REMARKS

The Applicants acknowledge the Office Action, a FINAL REJECTION, of May 3, 2007, which Final Rejection does not reflect that the applicant's remarks were given appropriate consideration. The Office indicates that Claims 11-18 are pending in the application and are presently under consideration.

The Applicants question the appropriateness of the Final Rejection under MPEP § 706.07 (c) and, at least, hereby request reconsideration and withdrawal of the finality of the instant Office Action. The repeated and arbitrary interpretation of the cited references, even after applicants identified such arbitrary interpretation is both prejudicial and inappropriate.

ENABLEMENT UNDER 35 U.S.C. § 112, FIRST PARAGRAPH:

The Office maintains the rejection of Claims 11-18 under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Office opines that the Specification is enabling for a method for treating a human or animal with 145-200 units of pure botulinum toxin; however, the Office concludes that the Specification does not enable administering doses of about 2500 units and above of botulinum toxin for treating a human or animal, which dosage is lethal.

While the applicants consider the Office rejection to be based on claim construction inconsistent with the instant claim to "treating", the applicants have amended Claims 11 and 16 to include the language, "administering, to the animal or human, a treatment effective amount of a botulinum neurotoxin...". The proposed claim recitation of a treatment effective amount, while redundant on the original claim to a method-of-treatment, necessarily excludes dosages of 2500 U or greater, which dosage is understood by those skilled in the art to be lethal (see the cited Gil, et al. and Carruthers, et al.). The Applicants submit that the amendment is responsive to the rejection for lack of enablement.

ANTICIPATION UNDER 35 USC § 102(b):

In the non-final Office Action of August 1, 2006, at page 7, the Office rejected Claims 16-18 under U.S.C. § 102(b) over the disclosure of Greene, et al. (Movement Disorders, Vol. 8, No. 4, 1993, p. 479-483) on the basis that Greene, et al. teach a method of treating patients with torticollis having immunity to botox type A.

The Office interpreted the instant claim language to neurotoxins "wherein the neurotoxin or mixture of neurotoxins is free of complexing proteins which naturally form complexes with botulinum neurotoxins" to mean "purified". Consequently, the Office concluded that Greene, et al. anticipate the instant invention because Greene, et al. teach that the botox type F was purified (page 480).

In the January 24, 2007 response to the rejection of Claims 16-18 as being anticipated by Greene, et al., the applicants distinguished the instant invention on the basis that:

1) the Greene, et al. disclosure pertains to the use of botox type F toxin complex as a replacement for botox type A toxin complex in patients who have developed neutralizing antibodies to botox type A toxin complex,

2) Greene, et al. does not disclose a botulinum neurotoxin which is free of the complexing proteins which naturally form complexes with botulinum neurotoxins, as recited in the generic claim and explained in the instant Specification.

It should be noted that in the Response of January 24, 2007 at page 4, the applicants highlighted Specificational description of the claim language; thereby, eliminating any ambiguity with regard to the claim language which is directed to "neurotoxins free of complexing proteins".

The Applicants explained that although the Office identified a statement in Greene, et al. that the botox F is "purified", the term as in Greene, et al. is not defined as a botulinum neurotoxin which is "free from complexing proteins" as instantly claimed and explained in the Specification. The applicants rebutted the rejection on the basis that written description of a neurotoxin, free from complexing proteins, i.e. hemagglutinins, is absent in Greene, et al. Consequently, the rejection for anticipation is not supported by the Greene, et al. disclosure and is nothing more than speculation on the part of the Office.

In the instant Final Rejection, the Office maintains the rejection of Claims 16-18 under 35 U.S.C. § 102(b) as being anticipated by Greene, et al. The Office indicates that the applicants' arguments were fully considered, but were not persuasive. The Office concludes that:

> "Green et al teach purified botulinum toxin type F. Applicant has not provided any evidence to suggest that the purified botulinum toxin type F as taught by Green et al includes complexing proteins. Therefore, this rejection is maintained."

The Office expands broadly on the disclosure that the botox F was "purified" to conclude that Greene, et al. anticipate claims to the use of a botulinum neurotoxin which is "free of complexing proteins", even though the term "purified" is never specifically defined in Greene, et al. to be a toxin which is free from complexing proteins. Such speculation can hardly be the basis for an anticipation rejection.

As stated in the above quotation from the instant Final Rejection, the Office maintains the anticipation rejection on the basis that the applicant has not provided any evidence that the term "purified" does not mean a "botulinum toxin free of complexing proteins". The applicants submit that the Office requirement that the applicant provide evidence of the teaching of the cited art is improper. The Office bears the burden of factually supporting the conclusion that a cited reference anticipates the claims, particularly in that the Office alleges an anticipation. The Office conclusion that the term "purified" as in Greene, et al. means a botulinum neurotoxin "free of complexing proteins" is not supported by any documentary evidence in the grounds of rejection. The Office maintains the rejection based it's own subjective interpretation of the term "purified".

Notwithstanding the Office arbitrary requirement that the applicants provide evidence that the term "purified" does not mean a botulinum toxin which is "free of complexing proteins", the applicants invite the Office to consider the disclosure of Carruthers, et al., cited in the instant Final Rejection, with respect to the understanding of those skilled in the art with regard to "purified" botulinum toxins. At page 210, Carruthers, et al. teach that:

> "Botox is a sterile, lyophilized form of botulinum toxin type A produced from a culture of the Hall strain of *C. botulinum* grown in a medium containing A-Z amine and yeast extract. It is purified from the culture solution by a series of acid precipitations to a crystalline complex consisting of a high-molecular-weight toxin protein and an associated hemagglutinin protein."

Carruthers, et al. teach that Botox®, a botulinum toxin with complexing proteins, is "purified" from the culture solution, which teaching supports the understanding of those skilled in the art regarding the term "purified" to describe the isolation of the toxin from the culture solution of *Clostridium botulinum*.

Moreover, the applicants provide the product literature for BOTOX®, which defines BOTOX® COSMETIC as (Botulinum Toxin Type A) Purified Neurotoxin Complex.

The applicants submit that the Office final rejection of the claims based on the Office subjective interpretation of the term "purified", concluding that the term "purified" means a botulinum toxin "free of complexing proteins" in the absence of any specific teaching in Greene, et al. or documentary evidence to support this conclusion, and the Office requirement that the applicants prove otherwise, is improper.

The applicants submit that written description of a neurotoxin free of complexing proteins, i.e. hemagglutinins, is absent in Greene, et al., and that the Office may not infer disclosure into the reference, especially in contrast to the teaching already of record. Consequently, the rejection for anticipation is not supported by the reference disclosure. Reconsideration and withdrawal of the rejection is respectfully solicited.

OBVIOUSNESS UNDER 35 USC § 103:

The Office maintains the rejection of Claims 11-12 and 14-15 under 35 U.S.C. § 103(a) as being obvious over the disclosure of Greene, et al. in view of Carruthers, et al. (Basic and Clinical Dermatology, Marcel Dekker, Inc., New York, Chapter 11, pages 207-236). The Office indicates that Greene, et al. teach a method of treating subjects with torticollis, and immunity to botox type A complex, with botox type F. The Office cites Carruthers, et al. for disclosing cosmetic treatment with botox type A complex and for suggesting that other botox serotypes can be used as alternative treatments for individuals who have developed antibodies to botox type A complex and no longer respond to treatment.

In the January 24, 2007 Response to the rejection in the non-final Office Action of August 1, 2006, the Applicants rebutted the obviousness rejection on the basis that the cited art do not teach or suggest all of the instant claim limitations, specifically, that Greene, et al. and Carruthers, et al. do not disclose or suggest a neurotoxin which is free from complexing proteins. Consequently, the Office rejection for *prima facie* obviousness is not literally made out.

With the instant Final Rejection, the Office states that the applicants' arguments in the January 24, 2007 Response were fully considered, but were not persuasive. It is the position of the Office that the applicant argued the references individually without clearly addressing the combination of teachings. The Office concludes that,

> "Green et al teach a method of administering purified botulinum toxin type F (without complexing proteins) to a patient that has developed neutralizing antibodies to botulinum toxin type A (includes complexing proteins). Carruthers, et al. teach that botulinum toxin type A (including complexing proteins) can be used to treat cosmetic conditions such as wrinkles and facial lines."

The Office basis for maintaining the rejection is that,

> "One would be motivated to use purified botulinum toxin type F to treat patients that have developed antibodies against botulinum toxin A (including complexing proteins) because Green et al has demonstrated that purified botulinum toxin F is a safe alternative to using botulinum toxin type A (including complexing proteins). There is nothing on the record to teach or suggest that the purified botulinum toxin type F as disclosed by Green et al includes complexing proteins. Therefore, this rejection is maintained."

As discussed previously, the Office has arbitrarily and capriciously interpreted the term "purified" botox F, as taught in Greene, et al., to mean "free of complexing proteins" but does not provide any documentary evidence to support the Office interpretation regarding the term "purified" over which the rejection is maintained.

The cited references do not disclose a botulinum neurotoxin which is free of the complexing proteins which naturally form complexes with botulinum neurotoxins, as recited in the generic claim and explained in the Specification. The applicants submit that written description of a neurotoxin free of complexing proteins, i.e. hemagglutinins, is absent in Greene, et al. and Carruthers, et al. Consequently, the

rejection for obviousness is not supported by the cited art. Reconsideration and withdrawal of the rejection is respectfully solicited.

Moving on, the Office maintains the rejection of Claim 13 under 35 U.S.C. § 103(a) as being obvious over the disclosure of Greene, et al. in view of Carruthers, et al. and further in view of Shelley, et al. The Office basis for the rejection is as stated above, with Shelley, et al. being cited for specifically teaching botulinum therapy for treating hyperhidrosis as in instant Claim 13.

In the applicant's January 24, 2007 Response to the rejection in the non-final Office Action of August 1, 2006, the applicants rebutted the obviousness rejection for the reasons discussed previously, in that the cited art do not disclose, nor suggest, administering a botulinum neurotoxin which is free of the complexing proteins which naturally form complexes with botulinum neurotoxins, as recited in the instant claims.

With the instant Final Rejection, the Office indicates that the applicants' remarks in the January 24, 2007 Response were fully considered, but were not persuasive. It is the position of the Office that the applicant argued the references individually without clearly addressing the combination of teachings. The Office concludes that,

> "Green et al teach a method of administering purified botulinum toxin type F (without complexing proteins) to a patient that has developed neutralizing antibodies to botulinum toxin type A (includes complexing proteins). Carruthers, et al. teach that botulinum toxin type A (including complexing proteins) can be used to treat cosmetic conditions such as wrinkles and facial lines. Shelley, et al. teach that botulinum toxin (including complexing proteins) can be used to treat patients suffering from hyperhidrosis."

The Office basis for maintaining the rejection is that,

> "One would be motivated to use purified botulinum toxin type F to treat patients that have developed antibodies against botulinum toxin A (including complexing proteins) because Green et al has demonstrated that purified

botulinum toxin F is a safe alternative to using botulinum toxin type A (including complexing proteins). There is nothing on the record to teach or suggest that the purified botulinum toxin type F as disclosed by Green et al includes complexing proteins. Therefore, this rejection is maintained."

As discussed previously, the Office has arbitrarily and capriciously interpreted the term "purified" botox F, as taught in Greene, et al., to mean "free of complexing proteins" but does not provide any documentary evidence to support the Office interpretation regarding the term "purified" over which the rejection is based.

In view of the foregoing, the applicants submit that written description of a neurotoxin free of complexing proteins as recited in the generic claim is absent in Greene, et al., Carruthers, et al., and Shelley, et al. Consequently, the rejection for obviousness is not supported by the cited art. Reconsideration and withdrawal of the rejection is respectfully solicited.

* * * * *

Accordingly, entry of the Response and Amendment After Final, Information Disclosure Statement, reconsideration of the finality of the rejection, reconsideration of all grounds of objection and rejection, withdrawal thereof, and passage of this application to issue are all hereby respectfully solicited.

It should be apparent that the undersigned attorney has made an earnest effort to place this application into condition for immediate allowance. If he can be of assistance to the Examiner in the elimination of any possibly-outstanding insignificant impediment to an immediate allowance, the Examiner is respectfully invited to call him at his below-listed number for such purpose.

Allowance is solicited.

Respectfully submitted,

THE FIRM OF HUESCHEN AND SAGE

By: 

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Enclosure: Listing of Claims; Extension of time fee, one (1) month, in the form a check in the amount of $120.00; Information Disclosure Statement, and fee in the form of a check in the amount of $180.00; accompanying references and Postal Card Receipt.

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THE COMMISSIONER IS HEREBY AUTHORIZED TO CHARGE ANY FURTHER OR ADDITIONAL FEES WHICH MAY BE REQUIRED (DUE TO OMISSION, DEFICIENCY, OR OTHERWISE), OR TO CREDIT ANY OVERPAYMENT, TO DEPOSIT ACCOUNT NO. 08,3220.